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Cofactors in the RNA World

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RNA world theories figure prominently in many scenarios for the origin and early evolution of life. These theories posit that RNA molecules played a much larger role in ancient biology than they do now, acting both as the dominant biocatalysts and as the repository of genetic information. Many features of modern RNA biology are potential examples of molecular fossils from an RNA world, such as the pervasive involvement of nucleotides in coenzymes, the existence of natural aptamers that bind these coenzymes, the existence of natural ribozymes, a biosynthetic pathway in which deoxynucleotides are produced from ribonucleotides, and the central role of ribosomal RNA in protein synthesis in the peptidyl transferase center of the ribosome. Here, we use both a top-down approach that evaluates RNA function in modern biology and a bottom-up approach that examines the capacities of RNA independent of modern biology. These complementary approaches exploit multiple *in vitro* evolution techniques coupled with high-throughput sequencing and bioinformatics analysis. Together these complementary approaches advance our understanding of the most primitive organisms, their early evolution, and their eventual transition to modern biochemistry.